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COMMENTS OF PHARMAVITE LLC ON PREMARKET NOTIFICATION FOR NEW DIETARY INGREDIENTS

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Pharmavite is a 33 year old company based in Los Angeles. We manufacture and market a broad line of dietary supplements comprised of vitamins, minerals, botanicals and a wide range of other dietary ingredients. Our products are sold in food, drug, mass merchandise and chain stores throughout the United States.

We are pleased that FDA is taking steps to clarify the regulatory requirements related to new dietary ingredients (NDIs) and we support FDA's efforts to develop a more structured framework for the submission of NDI notifications. As a result of these efforts, we believe consumers will benefit from a higher assurance of product safety and responsible companies will benefit from operating on a more level playing field resulting from a clearer understanding of these requirements.

We will submit more detailed written comments to the Docket on a variety of issues raised in the Federal Register Notice announcing today's meeting, but for today I would like to specifically address three important issues related to the topic. I will first address the types of changes that should influence whether an "old" dietary ingredient is considered "new"; secondly, the type of information that should be required in NDI notifications; and finally, some points about enforcement of the NDI notification provisions.

STATUS OF NEW DIETARY INGREDIENTS

Determining all of the variables that may impact whether a dietary ingredient is considered "new" is a difficult undertaking and no single answer will satisfy all situations. Furthermore, DSHEA does not clearly define the types of changes to a so-called "old" dietary ingredient that would result in a *new* dietary ingredient. Given the

broad diversity of substances that potentially qualify as dietary ingredients and the wide range of possible effects that ingested substances may have on the human system, we believe it is better to error on the side of caution when determining whether an ingredient is a *new* dietary ingredient and subject to FDA notification requirements.

Therefore, we believe that in many situations changes to the chemical composition or structure of an old dietary ingredient should cause the altered substance to become a *new* dietary ingredient. This would include modifications to existing ingredients that result in new salt forms, new esters, chelates, complexes and other chemically modified or stabilized forms of old ingredients. This reasoning would also extend to old ingredients produced through new or unique manufacturing processes if the new processes result in significant alterations to the composition or chemical structure of the old ingredients. Additionally, botanical ingredients obtained from plants used in dietary supplements before 1994, but obtained from parts of the plant not previously used should be considered new dietary ingredients. In contrast, old ingredients that undergo changes in their manufacturing process that do not alter the chemical structure of the ingredients should not be considered new ingredients. Such changes may include the use of different synthetic pathways to achieve the same ingredient or the use of different filtration or other purification techniques, but may not necessarily alter the basic chemical structure of the dietary ingredient.

NDI NOTIFICATIONS

While we support a broad interpretation of what constitutes a new dietary ingredient, we feel it is equally important that requirements for NDI notifications should be sufficiently comprehensive, but not overbearing. We believe that notifications should

contain sufficient information to clearly characterize the substance in question. As a general rule, more information is always preferred, but at a minimum, notices should include a clear description of the chemical structure of an ingredient containing a single compound and provide a reasonably complete characterization and profile of major constituents for more complex substances, such as fatty acid complexes and botanical extracts.

Recommendations for conditions of use by the consumer and the amount of the NDI contained in proposed dietary supplements should be clearly stated in the notice. However, the formulation of the dietary supplement and copies of the actual labeling of the product should not be required, because such formulations and labeling are frequently not developed at the time when notices are filed.

The level of evidence needed to establish a reasonable expectation of safety should remain reasonable and flexible. For instance, the nature and amount of evidence sufficient to satisfy a reasonable expectation of safety may vary according to the degree of knowledge about the composition of the substance or whether the NDI is closely related to other known substances with known characteristics. In cases where a modification to an old ingredient results in a new ingredient, required safety evidence should generally focus on the impact of the change in the new ingredient. We believe that appropriate data comparing the new form of ingredient to the existing ingredient generally should be sufficient for acceptance by FDA rather than the kind of data package needed for a completely new substance.

In order to reduce unnecessary burden on dietary supplement and dietary ingredient companies, we believe that FDA guidance should affirm that redundant NDI notices do not have to be submitted for ingredients for which another company has

already submitted a satisfactory notice. This assumes that the ingredient is essentially identical to and used for the same conditions of use specified in previous filings. For example, while data submitted by the ingredient manufacturer covers those who use and distribute the substance in dietary supplements, it should also be made clear that a submission by one distributor of a dietary supplement also covers the same use by other distributors of the same substance whether or not in the same chain of distribution. However, this is not to say that "one size fits all." Previous notice submissions should only be relied on if the levels of consumption and other conditions of use are consistent with the limitations specified in previous submissions. Where significant changes occur, new NDI notifications should be required for the new ingredient.

ENFORCEMENT

We also believe that enforcement of the NDI notice provisions is an important issue for FDA to begin address at this time. Consistent and evenly applied enforcement of NDI notice requirements will be a key factor in creating meaningful guidelines and a level playing field for manufacturers of dietary ingredients and dietary supplements. A number of products exist on the market today that contain NDI's for which NDI notices have not been filed. In some cases, the companies may either be ignorant of the notice requirements or have simply proceeded on the basis of liberal interpretations of the law. Unfortunately there are others who are blatantly cutting corners and exploiting a lenient enforcement environment. These situations have resulted in an unfair playing field for companies that attempt to uphold their end of the bargain. As one example, Pharmavite recently considered an opportunity to market a supplement that included what we believe is clearly a new dietary ingredient. Upon diligent review, we declined to market this

product because we did not feel that sufficient safety data exists at this time to submit a satisfactory NDI notification. We are therefore pursuing additional studies to verify the safety of this ingredient. However, others in this industry, including major competitors, have chosen to market this same product without filing an NDI notice. This obviously puts us in a significant marketing disadvantage.

We urge FDA to establish reasonable guidelines for NDI notices and to institute enforcement measures as soon as possible. Recognizing that FDA has limited resources to police this situation, we suggest that FDA consider using an enforcement approach similar to the issuance of "Courtesy Letters" for structure/function claims. Such letters have been used effectively to advise companies about FDA's interpretation of the regulatory requirements for dietary supplement claims. We believe that a similar approach could be effectively implemented to notify companies who have failed to meet their obligation to file NDI notices, without a large investment in time and resource by the agency.

CONCLUSION

To conclude, we believe it is in the long term best interest of consumers and of responsible businesses to carefully review the safety of all new dietary ingredients. We believe that a conservative approach is preferred when determining the status of new dietary ingredients. However, this should be balanced with reasonable and focused NDI notification requirements. Finally, efforts to enforce the NDI notice provisions will help assure broader compliance within the industry, promote a fairer marketing environment and ultimately help assure the availability of safer products for consumers.